

POLYGLYCEROLS AND POLYGLYCEROL ESTERS IN NUTRITION, HEALTH AND DISEASE

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Polyglycerols and polyglycerol esters, as a broad class of compounds, have been used for a number of years as useful and desirable adjuncts in nutrition, health, and in the treatment of certain diseases. The use of these compounds has been limited by their lack of quality and reproducibility in nutritional and medical products that would be submitted for approval to the Food & Drug Administration (FDA). With the process developed by Babayan and issued as U.S. Patent No. 3,637,774¹, this limitation was overcome. In recent years we have noted the availability of such products and the approval by the FDA and the Codex Alimentarius for the use of polyglycerol esters of fatty acids in foods.

The edible and industrial applications of the various polyglycerol esters are appearing in the literature, as well as products which list polyglycerol esters as one of the components in the formulation of the product. It is not surprising that a broad range class of compounds having multi-functionality and flexibility is being considered over an equally broad range of hydrophilic-lipophilic emulsification requirements. A study of their physical and chemical composition and properties is indicative of their unique and useful functionality and applications.

Although in previous presentations and publications²⁻¹² we have covered the salient characteristics of the polyglycerol esters, it may be useful to briefly summarize the data for the completeness of this presentation.

When glycine is subjected to heat in the presence of a catalyst, polymerization takes place. Usually the condensation takes place at temperatures above 200°C with the elimination of water and the formation of an ether linkage between two glycine molecules. Fig. 1 illustrates this reaction. The condensation reaction involves the α -hydroxyl groups of the glycerol molecule. Subsequent polymerization proceeds with the remaining α -hydroxyl groups and another glycerol molecule to form higher polymers. The reaction continues and the glycerol molecule has a range of polymerization. The reaction is followed by the changes in refractive index, viscosity and buoyant volume of the product. Some typical specific gravity and viscosity figures for a range of the polyglycerols is given in Table 1. The polyglycerols of the various polymer ranges are viscous fluids which are water soluble.

The polyglycerols may be converted into polyglycerol esters by direct esterification with a fatty acid or by intermolecular rearrangement with a triglyceride. The polyglycerol formed by the heat polymerization can now be reacted with fatty acids of varying chain length and unsaturation. Fatty acids

TABLE 1. Typical Viscosities and Specific Gravities of Commercially Prepared Polyglycerols

	Specific gravity	Viscosity, cs.	99°C
Polyglycerol	1.279	640	70
Triglycerol	1.283	1700	110
Hexaglycerol	1.290	3200	240

from acetic to tetracosenic in the saturated series and/or mono, di and polyunsaturated fatty acids such as oleic, linoleic and linolenic, etc. in the unsaturated series may be used in the direct esterification. The other alternative is to conduct molecular rearrangement with a triglyceride of known composition and structure a new polyglycerol ester at random distribution. Fig. 2 illustrates the two reactions that may be used in the preparation of the polyglycerol esters. Depending upon the molar ratios used in the reaction and the condition employed, one is able to prepare partial or neutral esters of polyglycerol of a given molecular weight and fatty acids and/or triglycerides of known composition. The polyglycerol esters prepared by these approaches constitute the basis for the diversified products that are available for edible, medical and industrial uses. R.T. McIntyre summarized the reactions and their product characteristics recently in an update on the polyglycerol esters¹³. The effect of the fatty acid chain length and degree of esterification on the hydrophilic-lipophilic balance (HLB) values of the polyglycerol esters is illustrated in Figs. 3, 4 & 5. The range of their specific gravities is given in Fig. 7. Their hydrophilic-lipophilic ranges is illustrated in Table 2. The wide range of the polyglycerol esters is clearly indicated in these figures and tables and once again re-emphasizes the flexibility and utility of the class as a whole.

Concurrently with the edible and industrial applications of the polyglycerol esters, several pharmaceutical, medical, nutritional and diabetic groups have been exploring the unique characteristics of the polyglycerol esters.

Since the polyglycerols are water soluble compounds and their viscosity increases with the increase in molecular weight, they become useful components in viscosity control, gravity control and humectants able to carry water and yet maintain the desired consistency of the food or medical formulation.

TABLE 2. HLB Values Calculated from the Theoretical Compositions of Products Formed by Reaction of Stearic Acid with Polyglycerols

	HLB		
	Molar Ratio of Stearic Acid : Polyol		
Polyglycerol	1:1	2:1	4:1
Triglycerol	6.71 (6.8)	4.91 (5.3)	2.6 (2.6)
Hexaglycerol	10.1 (10.2)	8.1 (8.6)	5.1 (5.1)
Decaglycerol	12.5 (12.5)	10.6 (11.2)	7.5 (7.5)

The partial esters of polyglycerols can be aerators or defoamers, emulsifiers, clouding agents, weighting agents and solvents for a variety of food product compositions. They tend to be multi-functional and do the work of several additives.

The U.S. Patent No. 4,093,750* demonstrates the suitability of such polyglycerol esters in the preparation of beverages. The multifunctional polyglycerol esters not only behave as solvents and carriers for flavoring agents, but also as stabilizers and clouding agents in such beverage preparations. Depending on the type of beverage desired, one can select the particular polyglycerol ester to bring out the desired characteristics.

The neutral esters of polyglycerols can be polymeric fats, lubricants, crystallization inhibitors, gloss additives, and more. They can also act as solvents and carriers for oil soluble vitamins, colors and other additives, as well as wetting agents.

The ability of polyglycerols and polyglycerol esters to replace fat in foods and yet maintain the safety and feeling of eating rich fatty foods has been utilized in special dietetic products, where more than 50% of the calories have been eliminated without sacrificing the consistency, appearance, and taste of the food. For example, the Weight Watchers Limitation Ice cream and dietetic dessert contains no fat, but uses the polyglycerol esters to give safety and to reduce the caloric content of the food.

Aside from the unique characteristics of being able to replace or eliminate fat from a formula, the polyglycerol esters also tend to reduce the actual caloric metabolic yield of a food. If we assume that the entire molecule of the polyglycerol mono-ester of a fatty acid is completely metabolized, a decapolyglycerol mono-ester for example, would contribute 5-6.3 kcal/g in contrast to the 9.2 kcal/g for fats. If, however, the polyglycerol backbone is not metabolized and only the fatty acid moiety is utilized, then the same compound would have less than 2 kcal/g. Fig. 8 illustrates the two cleavage points which are in question in the metabolic fate of the polyglycerols and polyglycerol esters. Our data has indicated that the polyglycerols and polyglycerol esters are quantitatively metabolized and utilized in both animal and human studies¹¹. Several other investigations, primarily Michaels and Conroy¹², have argued that the polyglycerol backbone is not completely metabolized. Using the largest polyglycerol molecule allowed by FDA, as the sole source of fat, decapolyglycerol was found in the urine of the test animals. As yet we do not know whether this finding represents excesses or the non-metabolized portion. In any event, all products appeared to be non-toxic.

The medical and pharmaceutical applications of the polyglycerols and the polyglycerol esters are an extension of the edible applications of these compounds, where the same functional characteristics can be utilized in medical formulations. In addition, they can be used as emulsifiers, solvents, and carriers for medications, the polyglycerol esters have demonstrated their unique solvency for carving liquids in various metabolic applications. In a conversation with W.G. Unsicker, MD (April 1981) the polyglycerol esters have acted as substitutes or as having a sparing action for patients with pancreatic insufficiency and bile acid insufficiency.

The medical and pharmaceutical applications of the polyglycerols and

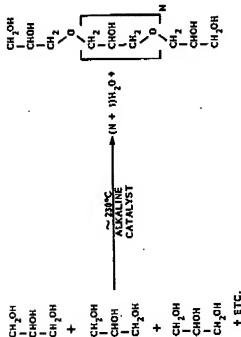


FIGURE 1. Preparation of polyglycol.

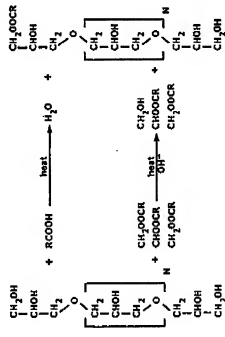


FIGURE 2. Partial ester formation.

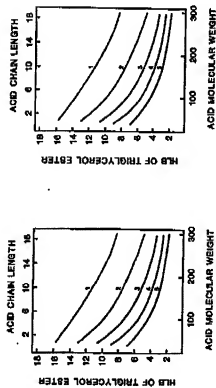


FIGURE 3. HLB of triglycerol ester vs. acid chain length and acid molecular weight.

FIGURE 4. HLB of triglycerol ester vs. acid chain length and acid molecular weight.

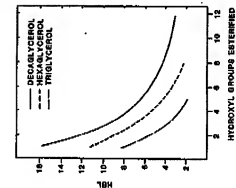


FIGURE 4. HLB of triglycerol ester vs. acid chain length and acid molecular weight.

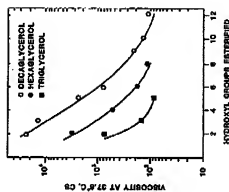


FIGURE 5. Viscosity of polytriglycerol.

FIGURE 6. HLB of triglycerol ester vs. acid chain length and acid molecular weight.

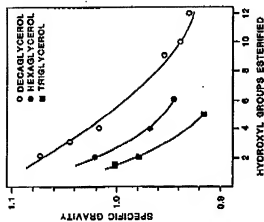
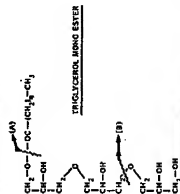


FIGURE 7. Specific gravity of polyglycerol esters.



(A): CLEAVAGE AT THE ESTER SITE IS WELL DOCUMENTED

(B): CLEAVAGE AT THE ETHER SITE IS NOW WELL DOCUMENTED. ETHER LINKAGES REQUIRE OMERIC BOILING WITH H₂O IN 10 TO 15% AQUEOUS SOLUTIONS FOR 12 HOURS. THIS HAS NOT BEEN DOCUMENTED. MINOR C-C BONDS (13-14) SHOWN ONLY FOR AN ENERGY SOURCE.

FIGURE 8. Possible modes of cleavage of polyglycerols and polyglycerol esters during metabolism in a living system.

polyglycerol esters are practically in their infancy. What has been done thus far is merely the extension of the edible applications. The future will see the polyglycerols and polyglycerol esters making a marked penetration into the medical, pharmaceutical and health care field because of their versatility and unique physical and chemical characteristics, which can be programmed at will to give the specific functionality desired.

Polyglycerols and polyglycerol ester applications and uses in the medical, health and disease areas were a natural extension of the knowledge we had acquired in the edible and industrial applications.

Grundy and Ahrens and others have used polyglycerol esters, notably the tri- and hexaglycerol oleates, as emulsifiers in special diets to solubilize and emulsify fat and cholesterol¹⁸. Such emulsions have proven to be very satisfactory in carrying the fat and cholesterol in a uniform and stable state. The polyglycerol esters have been suggested to the pharmaceutical field as a unique class of emulsifiers, which are suitable for emulsion preparations where fat, cholesterol or other medication is to be solubilized and/or carried. The oleates are liquid and the stearates are solid. Depending upon the type of product involved, one can select the specific polyglycerol ester best suited for the functionality. For example, the oleates are good solvents for cholesterol and other steroids and ring compounds, the stearates are good aerating agents and best suited for creams and ointments where aeration and volume is desired.

Other food preservatives in a series of publications have shown that the polyglycerols and polyglycerol esters are effective. Such anti-microbial properties are at an optimum with lauric acid and fall off either side of the fatty acid chain length. The anti-microbial properties of the polyglycerol laurates progressively increase as the molecular weight of the polyglycerol increases. Thus, tri-, hexa- and decaglycerol laurates show progressively greater anti-microbial power. The number of free hydroxyls apparently enhances the anti-microbial ability of the laurate ester.

In this connection the recent data that is beginning to be reported in the literature appears to point to the excess of the production of bile acids and their contact with colon tissues over prolonged periods of time. This increased exposure appears to increase the incidence of colonic cancer. Particularly in diets rich in fat, especially polyunsaturated fat, the incidences appear to be greater than that with diets having low fat content. If the polyglycerol esters can serve as a bile acid replacement and/or a sparing action, then they may be able to reduce the need for excessive bile acid production and the excessive concentrations appearing in the intestinal tract. Certainly the alternatives to the production and presence of high concentrations of bile acid in the colon should be helpful in reducing the instances of colonic cancer. We shall wait to see whether polyglycerol esters can play a useful role in this area.

This good solvent characteristic of the polyglycerol oleates for cholesterol has prompted some investigators to consider them not only as carriers and solvents for cholesterol, but also as possible agents for regression and solubilizer of atherosclerosis and plaque regression. W.C. Unsworth, MD and others (April 1981) have found polyglycerol esters, notably tri- and hexaglycerol mono-caprylate and oleate, to increase fatty acid transport through the intestinal wall, markedly enhancing fat utilization in patients requiring fat or caloric sup-

plementation. Linscheer also found that in patients deficient in or devoid of bile acids and/or pancreatic lipase, the polyglycerol esters were able to alleviate and/or slow sparring action for these substances. The possibility that polyglycerol esters may possibly substitute bile acids and pancreatic lipase was of great importance, and the need for much more clinical evidence is needed before we can assume that this type of polyglycerol esters in food products, however, may prove to be a help to patients having such deficiencies in bile acid and pancreatic lipase excretions.

In a conversation S.A. Hashim, J. Saleh and others (December 1990) have noted the beneficial effect of polyglycerol esters, namely the triglycerid mono-caprylate and the deca-glycerol mono-laurate in the absorption and transport mechanism in humans. In some ways their work is collaborative to that carried out by Linscheer and extends the area of utilization of the polyglycerol esters. Hopefully other experimental data will become available to confirm other such unique uses of the polyglycerol esters.

The anti-microbial, emulsification and solvent action of polyglycerol caprylates and laurates presents the possibility that such products can be considered as emulsifiers and protective agents for intravenous preparations, where sterility and protection against bacterial infection is always a desired state. Alone or with egg phosphatides, such polyglycerol laurates may well serve to improve parenteral fat emulsions.

In the area of dietetic formulations where caloric restriction is required, the polyglycerol esters can serve as hybrid fats or as low calorie food product, even when used as the sole source of fat in a balanced diet. Babayan has postulated that such polyglycerol esters can play the role of a dietetic fat not only because the caloric value of the polyglycerol mono-esters are in the range of 6-6.5 calories, but also because one can formulate products devoid of fat or very low level of fat, and yet give the impression that one is eating a rich fatty food. The palatability and satiety factor of such products is very acceptable.

Some questions have been raised by Michael and Coats whether the polyglycerol backbone is metabolized. Our data submitted to the FDA, for the clearance of such product in food use, showed that polyglycerols are completely metabolized. In the event, however, that the contention of Michael and Coats proves to be valid, such polyglycerol mono-esters would have less than 2 calories instead of 6-6.5 cal/energy. Thus, these low calorie emulsifiers would be even more useful for low calorie dietetic foods.

In all, the polyglycerol esters for consideration as a medical and physiological tool, as well as a nutritional and dietetic food component promises to be a very fertile area of investigation and development. It remains for the physicians, clinicians, and dietitians to increase our knowledge with their investigative results.

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